IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	**Young Mi Choi-Sledeski, et al.**		
Application No.:	**09/918,039**	Examiner:	**T.N. Truong**
Filed:	**July 30, 2001**	Group Art Unit:	**1624**

For: **SULFONIC ACID OR SULFONYLAMINO N-(HETEROARALKYL) AZAHETERYCYCLYLAMIDE COMPOUNDS**

Attorney Docket No.: **P24,450-E US1**

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June 30, 2006 Peter J. Butch III

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PETITION UNDER 37 C.F.R. § 1.144 REQUESTING WITHDRAWAL OF RESTRICTION REQUIREMENT

Sir:

This is a request that a Restriction Requirement made by the U.S. Patent and Trademark Office relative to the above-identified application be withdrawn. Payment of the requisite petition fee ($130.00) under 37 C.F.R. §1.17(h) is enclosed.

Claims

Claims 35-41 are pending in the instant application. These claims are attached hereto as "Attachment A." Claim 35 is an independent claim directed to a method for treating a patient suffering from a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa by administering to the patient a therapeutically effective amount of an aminopyrrolidinone-pyrrolopyridine Factor Xa-inhibiting compound

according to the claimed formula. Claims 36 and 37 depend from claim 35. Claim 39 is an independent claim directed to a pharmaceutical composition for treating a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa comprising a therapeutically effective amount of a Factor Xa-inhibiting aminopyrrolidin-one-pyrrolopyridine compound of the claimed formula and further comprising in a separate or combined formulation at least one other agent selected from diagnostic agents, cardio-protective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinolytic agents . Claims 40 and 41 depend from claim 39.

Restriction Requirement

In the Restriction Requirement, which was mailed June 27, 2005, the Examiner restricted the claims of the application between Groups I-XVI. A copy of the Restriction Requirement is attached hereto as "Attachment B." In particular, the Examiner did not divide claims 35-41 between treatment method claims 35-38 and pharmaceutical composition claims 39-41. All 16 claim groups are directed to both pharmaceutical compositions and treatment methods using compounds having the same structural formula. Instead, each claim group is directed to the combined treatment method and pharmaceutical composition subject matter of claims 35-41 and restricted according to structural features of the active compound used in the treatment method and pharmaceutical composition.

Applicant's Response to Restriction Requirement

In a paper filed September 22, 2005 entitled, "Reply Pursuant to 37 C.F.R. §1.111," Applicants traversed the Restriction Requirement arguing that it was improper and requesting reconsideration and withdrawal. Applicants provisionally elected Group XVI and elected as a species within that group thieno(3,2-b)pyridine-2-sulfonic acid(2-oxo-1-(1H-pyrrolo)(2,3-c)pyridine-2-methyl)-pyrrolidine-3-S)-yl)-amide, depicted an Example 48. A copy of Applicant's response to the Restriction Requirement is attached hereto as "Attachment C."

Office Action

The Examiner made Restriction Requirement final in an Office Action dated December 30, 2005. A copy of the Office Action is attached hereto as "Attachment D." Claim Group XVI was further restricted into Groups XVIa and XVIb. The Examiner proceeded to examine Group XVIa. Future further Restriction of Group XVIb was not ruled out.

For the reasons given below, Applicants submit the Restriction Requirement is improper and should be withdrawn.

I. SUMMARY

The Restriction Requirement considered the common core structural feature of the claim compounds to be an aminopyrrolidinone-pyrrolopyridine, stating that the pyrrolidinone ring alone did not sufficiently define the invention. According to the Restriction Requirement, the variation of the position of the nitrogen atom within the pyrrolopyridine ring structure and the R_2 substituent on the pyrrolidinone amino group gave the compounds restricted to each claim group "distinct physical, chemical and/or biological properties." According to the Restriction Requirement this set apart the compounds of one group from another and required a separate search for each group that, without Restriction, "would impose a serious burden upon the Examiner."

According to MPEP § 803.02, "(i)f the members of the Markush a group are sufficiently few in number or so closely related that a search and examination of an entire application of the entire claim can be made without serious burden, the Examiner must examine all the members of the Markush a group in the claim on the merits, even though they are directed to independent or distinct inventions." In the present application, Applicant submit that the search directed to all pyrrolopyridine compounds, regardless of the positions of the nitrogen atoms, would not pose an undue burden, particularly as the members of the pyrrolopyridine Markush group are "sufficiently fueling number." In addition, as discussed in greater detail below, the Restriction Requirement also supports Applicant's position that the Examination of all pyrrolopyridine rings can be made without serious burden as it shows significant overlap in the classification between the individual members of the Groups designated by the Examiner.

In the Restriction Requirement, the Examiner divided Applicant's seven claims into sixteen groups. Applicants submit that this is an excessive number of groups, particularly in view of the small number of pyrrolopyridine Markush group members.

Applicants submit that such an excessive number of Groups is prejudicial to Applicants partly because of the cost involved in filing additional patent applications and maintaining additional patents. Moreover, a 17th Group has already been carved out of Group XVI and may be subject to further Restriction. The pyrrolopyridine rings represents subject matter the elective an earlier 17-ring restrictive requirement that the present restrictive requirement presents a further Restriction.

Such an excessive number of Groups is also prejudicial to Applicants because the resulting high number of patents offer less effective protection than a fewer number of patents or a single patent. Applicants further submit that an excessive number of Groups is also prejudicial to the public interest because the notice function of 34 or more patents is less effective than that of a fewer number of patents or a single patent. Specifically, it is much more difficult and time-consuming to review 34 or more patents than it is to review a smaller number of patents or a single patent.

Thus, Applicants respectfully submit that the Restriction Requirement is improper and should be withdrawn because a search and examination of all pyrrolopyridine rings in a single application can be made without serious burden, and separatingthe claimed invention into 34 groups is excessive and prejudicial to Applicants and to the public.

II. BACKGROUND: THE RESTRICTION REQUIREMENT BETWEEN GROUPS I-XVI

In the Restriction Requirement, the compounds to which independent treatment method claim 35 and independent pharmaceutical composition claim 39 are directed were divided 16 ways along two Markush groups. In particular, the compounds were divided according to the members of the pyrrolopyridine Markush group and the members of the Markush groups of the R_2 amino substituent on the aminopyrrolidinone moiety.

Groups I-V were based on treatment methods and pharmaceutical compositions using the compounds of the claimed formula in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anti-coagulant agents, antiplatelet agents and fibrinoloytic agents, in which the pyrrolopyridinyl ring is pyrrolo(2,3-c)pyridine and R_2 is:

Group I-	SO_2 –phenyl or SO_2-naphthyl
Group II-	SO_2-(five-memberheteroaryl or heterocyclyl)
Group III-	SO_2-(six-memberheteroaryl)
Group IV-	SO_2-Quinolinyl
Group V-	SO_2-Benzopyranyl

Groups VI-X were based on treatment methods and pharmaceutical compositions using the compounds of the claimed formula in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinoloytic agents, in which the pyrrolo-pyridinyl ring is pyrrolo(2,3-c)pyridine. Groups VI-X were further divided according to the R_2 amino substituent the same way the R_2 amino substituents were divided for Groups I-V.

Groups XI-XV were based on treatment methods and pharmaceutical compositions using the compounds of the claimed formula in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinoloytic agents, in which the pyrrolo-pyridinyl ring is pyrrolo(3,2-c)pyridine. Groups XI-XV were further divided according to the R_2 amino substituents the same way the R_2 amino substituents were divided for Groups I-V and Groups VI-X.

Group XVI was based on treatment methods and pharmaceutical compositions using the compounds of the claimed formula in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anti-coagulant agents, antiplatelet agents and fibrinoloytic agents, in which the combination of pyrrolopyridine ring and R_2 amino group is not in Groups I-XV.

In the Restriction Requirement, the Examiner stated that invention Groups I-XVI were distinct, each from the other, because of the following reasons:

> a. Invention Groups I-XVI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP §806.04, MPEP § 808.01). In the instant case the combination of rings represented by Ar^1, R_2 and the pyrrolidinone ring define the

different inventions.

b. Although all groups share the ring of *pyrrolidinone,* said ring alone does not sufficiently define the invention, and does not contribute to the art. Therefore, it is the combination of the *pyrrolidinone* Ar^1 and R_2 that gives each group a distant physical, chemical and/or biological properties, and thus sets apart the compounds of one group from those of the others. Thus, a reference that anticipated, or rendered obvious one Group could not do so to the others, and so, a separate search is required for each group.

Because the inventions are distinct for the reasons given above and the search required for Group I is not required for Group II – (16), and the search for all (16) distinct invention(s) impose a serious burden upon the Examiner in charge on this invention, Restriction for the examination purposes as indicated is proper.

In response to Applicants' argument that there was no basis for Restriction because the compounds have a substantial structural feature represented by the pyrrolopyrridine ring and a common utility, the Examiner, in the Office Action making the Restriction Requirement final, stated that the argument was not persuasive for the following reasons:

The *bicyclic* core of A_1-A_4 can vary in structure depending on the position of A_1- A_3. The core of *pyrrolo(2,3-b)pyridine* is definitely not obvious over the core of *pyrrolo(3,2-c)pyridine*, nor is it obvious over *pyrrolo(2,3-c)pyridine*. Therefore, the bicyclic core is not a special technical feature that is common to compounds of all the groups.

Furthermore, variables R_1 and R_2 represent a large number of functional groups and ring systems(, t)he combination of which would definitely set apart compounds of one groups from those of the others.

Although all groups share the *pyrrolidinone* ring, such a ring alone does not sufficiently define the invention, and is not a contribution to the art.

Therefore, it is the combination of at least *pyrrolidinone, bicyclic core* and R_2 that gives compounds in each group their unique physical and chemical properties as well as biological activity.

The Examiner then went on to divide elected Group XVI between (1) Group XVIa containing the treatment methods and pharmaceutical compositions of claims 35-41 using the compounds of the claimed formula in combination with at least one other agents selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anti-coagulant agents, antiplatelet agents and fibrinoloytic agents, in which the pyrrolopyridinyl ring is pyrrolo(2,3-c) pyridine, R_2 is $R_3S(O)p$ wherein p=2; R_3 is thieno(3,2-b)pyridine and

X_3 and one of X_1 and X_{1a} do not form a fused pyrrolidinone ring; and (2) Group XVIb containing the treatment methods and pharmaceutical compositions of claims 35-41 using the compounds of the claimed formula in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin and inhibiting agents, anti-coagulant agents, antiplatelet agents and fibrinoloytic agents, in which the pyrrolopyridinyl ring is not pyrrolo(2,3-b)pyridine, pyrolo(3,2-c)pyridine or pyrolo(2,3-c)pyridine; R_2 is not $R_3S(O)p$, wherein p=2; and R_3 is not thieno(3,2-b)pyridine.

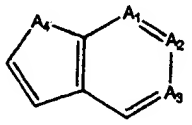
Because the elected species fell within Group XVIa, the Examiner elected this group for consideration and withdrew from consideration the subject matter of Group XVIb.

III. ARGUMENTS: THE RESTRICTION REQUIREMWNT BETWEEN GROUPS I-V, VI-X and XI-XV SHOULD BE WITHDRAWN

A. Search and Examination of the Compounds of the Claimed Formula Can Be Made Without Serious Burden

According to the Examiner, a search of all 16 claim groups would impose a serious burden because the compounds contained in each group are independently patentable and distinct from each other. Applicants submit that a search directed to the aminopyrrolidinone-pyrrolopyridine core identified by the Examiner will not pose a serious burden because there is no wide variation in the pyrrolopyridine substituent group restricted by the Examiner.

The pyrrolopyridine group is limited to a fused ring structure having the formula:



Wherein one of A_1, A_2 and A_3 is N, the other two are CH, and A_4 is NR_1. The Examiner considers variations in the positioning of the heteroatoms around the pyrrolopyridine ring coupled with variations in the R_2 moiety to encompass compounds that "are not disclosed as capable of use together and. have different modes of operation, different functions or different effects." On this basis, the Examiner concludes that the 16 claim groups are patentably distinct, and Restriction proper because of the burden imposed by searching all 16 groups.

Applicants respectfully disagree that the inventions have different modes of operation and function and different effects. The inventions defined in the claims of Groups I-XVI have a common utility, Factor Xa inhibition. While there may be patentable distinction among the compounds, the claim groups identified by the Examiner are not independent.

This is particularly striking with respect to claim Groups I, VI and XI, claim Groups II, VII and XII, claim Groups III, VIII and XIII, etc., in which the claimed compounds vary only by the positioning of the heteroatom around the pyrrolopyridine ring. Rearrangement of heteroatoms within a ring structure does not give rise to an independent invention. Nor do claim Groups I-V, VI-X and XI-XV represent independent inventions. Each five groups of claims vary only by a single amino substituent on the pyrrolidinone ring. Such a minor substituent variation also does not create independent inventions.

Moreover, the Examiner has not attempted in the Restriction Requirement to explain why he considers the claims to be directed to independent inventions other than to make an unsupported conclusory statement that the compounds as grouped are independent. It is submitted further that a proper search of the subject matter of each claim group requires a search be conducted for the subject matter of all groups of claims. This is because the subject matter of the claims is so interrelated. For example, Groups I, VI and XI are drawn to compounds wherein in each compound R_2 is SO_2-phenyl or SO_2-naphthyl. The difference between the Group I, VI and XI compounds is that the pyrrolopyridine group is pyrrolo(2,3-c)pyridine, pyrrolo(2,3-b)pyridine or pyrrolo(3,2-c)pyridine. According to the Restriction Requirement, the compounds of all three groups are classified in classes 514 and 546 and thus involve the same field of search.

Similarly, Groups II, VII and XII are drawn to compounds wherein in each compound R_2 is SO_2-(five-member heteroaryl or heterocyclyl) and vary by the pyrrolopyridinyl group being pyrrolo(2,3-c)pyridine, pyrrolo(2,3-b)pyridine or pyrrolo(3,2-c)pyridine. According to the Restriction Requirement, the compounds of all three groups are classified in classes 514 and 546 and thus also involve the same field search.

Furthermore, Groups III, VIII and XIII are drawn to compounds wherein in each compound R_2 is SO_2-(six-member heteroaryl) and vary only by the pyrrolopyrinyl group being

pyrrolo(2,3-c)pyridine, pyrrolo(2,3-b)pyridine or pyrrolo(3,2-c)pyridine. According to the Restriction Requirement, the compounds of all three groups are also classified in classes 514 and 546 and thus also involve the same field of search as Groups I, II, VII, VII, XI and XII.

Likewise Groups IV, IX and XIV are drawn to compounds wherein in each compound R_2 is SO_2-quinolinyl and vary by the pyrrolopyridinyl group again being pyrrolo(2,3-c)pyridine, pyrrolo(2,3-b)pyridine or pyrrolo(3,2-c)pyridine. According to the Restriction Requirement, the compounds of all three groups are also classified in classes 514 and 546 and thus involve the same field of search as the compounds of Groups I-III, VI-VIII and XI-XIII.

Finally, Groups V, X and XV are drawn to compounds wherein in each compound R_2 is SO_2-benzopyranyl and vary by the pyrrolopyridinyl group again being pyrrolo(2,3-c)pyridine, pyrrolo(2,3-b)pyridine or pyrrolo(3,2-c)pyridine. According to the Restriction Requirement, the compounds of all three groups are also classified in classes 514 and 546 and thus involve the same field of search as the compounds of Groups I –IV, VI – IX and XI – XIV.

Significantly, all 16 groups identified by the Examiner are classified in classes 514 and 546 and all involve the same field of search. Thus, Applicants submit that a search directed to the compounds of Groups I-XVI will not pose a serious burden to the Examiner and that the compounds of these groups for this reason should be contained in a single Application.

B. <u>The Compounds of the Claimed Formula Have "Unity of Invention"</u>

MPEP § 803.02 provides that there is no basis for requiring Election or Restriction of Markush-claimed invention when two factors are met, i.e.:

> ... unity of invention exists where compounds included within a Markush Group (1) share a common utility and (2) share a substantial structural feature ... essential to that utility.

For the reasons given below, Applicants submit that the embodiments of the compounds of the claimed formula separated into Groups I-XVI (a) share a common utility and (B) share a substantial structural feature essential to that utility.

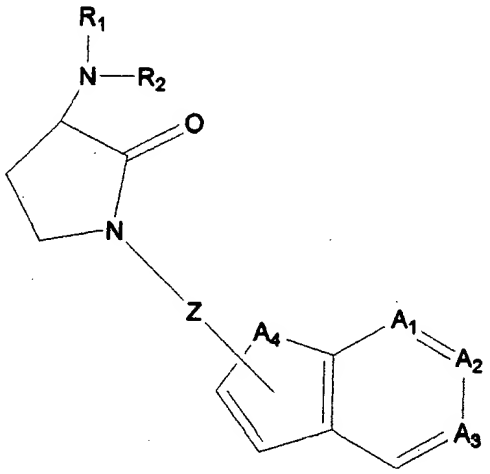
<u>Common Utility</u>

The compounds of the claimed formula are useful for treating physiological disorders modulated by inhibiting an activity of Factor Xa. Because all the compounds of the claimed

formula as set forth in claims 35-41 have the foregoing utility, the embodiments of these compounds separated into Groups I-XVI "share a common utility."

Substantial Structural Feature

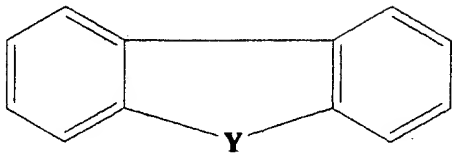
The compound of the claim formula have the following substantial structural feature identified by the Examiner:



The foregoing structure defines a common nucleus having a community of properties, wherein the claimed structure is a pyrrolidinone linked by a divalent "Z" to a pyrrolopyridine fused ring structure that can vary isomerically. Applicants submit that variation among location of nitrogen atoms in the pyrrolopyridine fused ring structures and the pyrrolidinone R_2 side groups does not provide an adequate basis for Restriction because, despite such variation, a genus can still be identified having a community of properties (Factor Xa inhibition) that justify the grouping all having the same structural feature essential to that utility.

Furthermore, the grouping of compounds having the same nuclei but side chains wherein there is wide variation is proper if the compounds all belong to the same genus having a community of properties justifying their grouping, In re Harnisch, 206 U.S.P.Q. 300, 305(CCPA 1980). Thus, the present Election and Restriction Requirements are improper because they seek election among substituents attached to a common nucleus defining a genus of compounds with a community of properties.

In Ex parte Dahlen and Zwilgmeyer, 42 U.S.P.Q. 208 (Bd. App. 1938), a Markush compound of the formula:



was found to be proper when Y was defined as a bivalent bridge radical that was further defined in Markush format as consisting of following 12 members:

-CH_2, -CO-, -C=C-, -CH_2CH_2-, -NH-, -N-Alkyl, -O-, -S-, -N=N-, -N=NO-, -SO_2-, -COCO-

The Markush grouping was found to be acceptable even though the variable "Y" provided for variations in the size and classes of the tricyclic ring system, i.e., the central ring can be defined to have a ring size of five or six members that includes a ring selected from a cyclopentadienyl ring, a cyclohexadienyl ring, a phenyl ring, and one of four different heteroaryl rings (pyrrolyl, furanyl, thienyl or pyridazinyl). This demonstrates that the present Restriction among pyrrolopyridinyl ring isomers based upon the position of the nitrogen atoms is improper because it gives rise to exceptionally less variability in the classes of compounds and encompassed by the genus defined by the core pyrrolidinone ring and the variations in the R_2 and pyrrolopyridine substituents. Accordingly, Applicants submit that Ex parte Dahlen and Zwilgmeyer supports that there is no basis for Election or Restriction in the instant case even though there is variability among pyrrolopyrdine fused ring isomers based on the position of the nitrogen atoms in the pyrrolopyridine fused ring.

Furthermore, the fact different fields of search are involved does not establish that Restriction of the Markush Group is proper. In Ex parte Brouard et al. 201 U.S.P.Q. 538 (Bd. Ap. 1976), six different fields of search were not deemed sufficient to establish proper Election or Restriction of the Markush group therein. Because there are only two different fields (classes 514 and 546) related to the presently restricted Groups I-XVI of the invention, this should not be viewed as providing proper basis of support for either Election or Restriction.

Applicants also submit that the applicable standard under which claims subject to Restriction are evaluated should not include whether there will be a serious burden on the

Examiner were Restriction not required, as suggested by MPEP §803[1]. Rather, the standard should align with the holding of In re Harnisch, wherein grouping of compounds having the same nuclei but widely-varying side chains is proper if the compounds all belong to the same genus having a community of properties with a common utility with an essentially common structural feature essential to that utility justifying their grouping.

Finally, the PTO Board of Appeals has held that there is no basis for a Markush rejection where the "Examiner dissects the molecule into core and pending substituents and then concludes that the variable core inherently constituted an improper Markush group," Ex parte Holt and Randell , 214 U.S.P.Q. 381, 386 (Bd. App. 1982). This is consistent with In re Harnisch's requirement that Markush Grouping analysis be conducted based upon a molecule "as a whole," and not as separately dissected parts of an invention, or separately dissected sections of claims, when analyzing Markush-type claims.

In summary, because the pyrrolopyridine ring is part of the common structural core identified by the Examiner and the isomers claimed do not vary widely, Restriction is improper pursuant to In re Harnisch. Because R_2 is a substituent of the common structural core identified by the Examiner, and because variation among the R_2 groups does not affect the common properties with a common utility or the essentially common structural feature essential to the utility of the compound grouping, Restriction among the R_2 groups is also improper pursant to In re Harnisch. Thus, for at least the foregoing reasons, Applicants respectfully submit that the Restriction Requirement between Groups I-XVI should be withdrawn and Groups I-XVI should be examined as a single application.

C. The Restriction Requirement on the Basis of Pyrrolopyridine Ring Structure Variation Should be Withdrawn.

The only difference between the embodiments of Groups I-V, Groups VI-X and Groups XI-XV is the position of nitrogen atom within the pyrrolopyridine ring structure. As noted above, Ex parte Dahlin and Zwilgmeyer supports that there is no basis for Election or

[1]See MPEP §803, Restriction When Proper states: "If the search and examina-tion can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. CRITERIA FOR RESTRICTION BETWEEN PATENTABLY DISTINCT INVENTIONS. There are two criteria for proper requirement for Restriction between patentably distinct inventions: (A) The inventions must be independent (See MPEP §802.01, §806.04, §808.01) or distinct as claimed (See MPEP §806.05-§806.05(i)); and (B) there must be a serious burden on the Examiner unless Restriction is required (See MPEP §803.02, §806.04(a)- §806.04(i), §808.01(a) and §808.02))

Restriction in the instant case on the basis of variability of nitrogen atoms among pyrrolopyridine fused ring isomers.

Thus, for at least the foregoing reasons, Applicant respectfully submit in the alternative that the Restriction Requirement between Groups I-V, Groups VI-X, Groups XI-XV and Group XVI be withdrawn and be replaced with a six-way Restriction Requirement based upon the R_2 moiety groupings identified in the Groups I-V and XVI.

D. The Restriction Requirement on the Basis of R_2 Rings Substituent Variation Should be Withdrawn.

The only difference between the embodiments within Groups I-V (and also within Groups VI-X and Groups XI-XV) is the R_2 ring substituents. As pointed out above, variations in the R_2 ring substituents do not provide adequate basis for Restriction (In re Harnisch) because, despite such variation, a genus of compounds can still be identified having a community of properties with a common utility and an essentially common structural feature essential to that utility that justify their grouping.

Thus, for the foregoing reasons, Applicant respectfully submit in the alternative that the Restriction Requirement between Groups I-V, Groups VI-X, Groups XI-XV and Group XVI on the basis of the R_2 ring substituent should be withdrawn and replaced with a four-way Restriction Requirement based upon the pyrrolopyridine moiety groupings identified in Groups I, VI, XI and XVI.

IV. CONCLUSION

For the above reasons Applicants respectfully request that the Restriction Requirement between Groups I-XVI be withdrawn and that claims 35-41 be searched and examined in their entirely in a single application.

Respectfully submitted,

June 30, 2006

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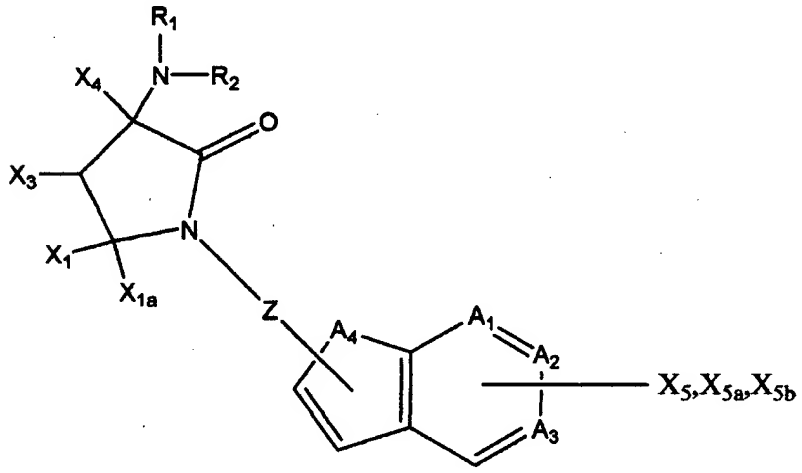
Attachment A

Pending Claims

35. A method for treating a patient suffering from a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa comprising administering to the patient a therapeutically effective amount of a Factor Xa-inhibiting pyrrolopyridine compound having the formula:



wherein Z is bonded to a pyrrolopyridine ring carbon atom, and one of X_5, X_{5a} and X_{5b} is an H, hydroxy, or amino substituent on the ring proximal to Z and attached at a carbon position that is adjacent to the carbon atom to which Z is attached and another of X_5, X_{5a} and X_{5b} is a substituent on the ring distal to the carbon atom to which Z is attached at a position alpha to the nitrogen on the distal ring and is selected from the group consisting of H, hydroxy, H_2N-, and (lower alkyl)HN-, wherein the lower alkyl is optionally substituted with an alkyl group substituent, (hydroxy)HN-, (alkoxy)HN- or (amino)HN-, the remaining one of X_5, X_{5a} and X_{5b} is a subsituent, as defined below, bonded to any one of the remaining carbon atoms of the pyrrolopyridine ring;

one of A_1, A_2 and A_3 is N and the other two are CH;

A_4 is NR_{11} and R_{11} is H, alkyl, aralkyl, heteroalkyl or $R_8(O)CCH_2$-;

Z is alkenyl, $-(CH_2)_r-C(O)NR"(CH_2)_s-$, $-(CH_2)_r-R"NC(O)(CH_2)_s-$ or $-(CH_2)_r-NR"(CH_2)_s-$, wherein R" is selected from the group consisting of : (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl position with one or more ring system substituents and optionally substituted in the alkenyl proportion with one or more substiuents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl proportion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, wherein "r" is selected independently for each occurrence from 1 and 2 and "s" is selected independently for each occurrence from 0, 1, and 2;

R_1 is selected from (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) alkenyl, optionally substituted with one or more substituents selected from halogen and cycloalkyl; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (e) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) a member of the group consisting of $R'O(CH_2)_x-$, $R'O_2C(CH_2)_x-$, $R'C(O)(CH_2)_x-$, $Y^1Y^2NC(O)(CH_2)_x$, and $Y^1Y^2N(CH_2)_x-$, wherein Y^1 and Y^2 are independently: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) heteroaryl, optionally substituted with one or more ring system; (e) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) heteroaralkyl, optionally substituted in the

heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 member heterocyclyl, R'is (a) hydrogen; (b) alkyl optionally substituted with one or more alkyl group substituents; (c) aryl optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl portion with one or more ring systems substitutents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally syubstituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, and x=1,2,3,4 or 5;

R_2 is selected from: (a) hydrogen; (b) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (c) heteroaralkyl, optionally substitu-ted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (d) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selective from halogen and cycloalkyl; (e) heteroaralkenyl, optionally substituted in the heteroaryl por-tion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (f) a member of the group consisting of $R_3R_4NC(O)(CH_2)_x$-, $R_3S(O)p$-, and $R_3R_4NS(O)p$-, wherein: x is selected from 1, 2, 3, 4 and 5, and p is selected independently for each occurrence from 1 and 2;

R_3 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroarayl; (d) heterocyclyl, optionally substituted with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl and fused hetero-aryl; (e) aryl, optionally substituted with a ring system substituent; (f) heteroaryl, option-ally substituted with a ring system substituent; (g) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (h) heteroaralkyl, optionally sub-stituted in the heteroaryl portion with one or more rings system substituents and optional-ly substituted in the alkyl portion with one or more alkyl groups substituents; (i) aral-kenyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (j) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl, or, optionally, R_1 and R_3 taken together with the –NS(O)p-moiety, the -S(O)p- moiety or the $-NR_4$- moiety through which R_1 and R_3 are linked form a 5 to 7 member heterocyclyl optionally substituted with one or more members selected from the group consisting of alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl substituents; and

R_4 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroaryl; (d) aryl, optionally substituted with a ring system substituent; (e) heteroaryl, optionally substituted with a ring system substituent; (f) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) hetero-aralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl group substituents, or, optionally R_3 and R_4 taken together

with the nitrogen to which R_3 and R_4 are attached form a 4-7 member heterocyclyl, optionally substituted with one or more substituents selected from halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl;

X_1 and X_{1a} are independently selected from: (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents; (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, X_1 and X_{1a} taken together from oxo;

X_3 is selected from: H; (b) hydroxyl; (c) alkyl, optionally substituted with one or more ring system substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents, (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl groups substituents, or, optionally, X_3 and one of X_1 and X_{1a} taken together from a 4-7 member cycloalkyl;

X_4 is selected from (a) H; (b) alkyl, optionally substituted with one or more alkyl

groups substituents; and (c) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents;

one of X_5 and X_{5a} and X_{5b} which has not been otherwise selected is selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, R_5R_6NSO2-,
R_7CO-, halo, cyano, nitro and $R_8(O)CCH2$-;

R_5 and R_6 are independently selected from (a) H and (b) lower alkyl, optionally substituted with one or more alkyl group substituents; or one of R_5 and R_6 is H and the other is $R_8(O)CCH2$- or lower acyl;

R_7 is H, lower alkyl optionally substituted with one or more alkyl group substituents or $R_8(O)CCH2$-;

R_8 is selected from H, lower alkyl substituted with one or more alkyl group substituents, alkoxy and hydroxyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

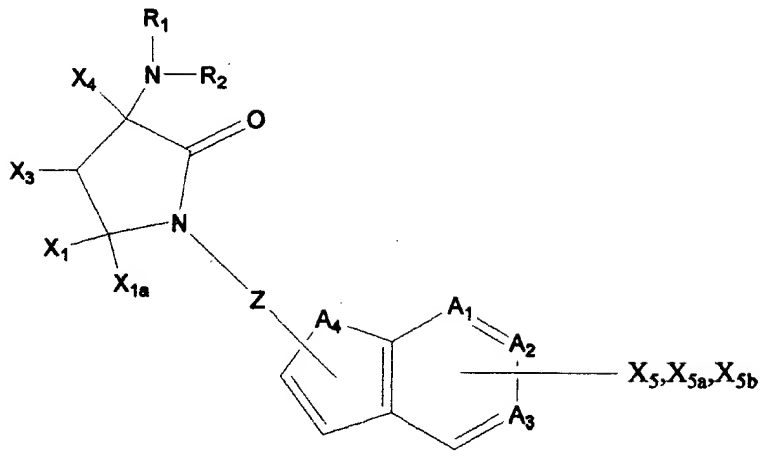
wherein said compound is administered in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinoloytic agents.

36. The method of claim 35 wherein said other agent is selected from standard heparin, low molecular weight heparin, direct thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

37. The method of claim 36 wherein said other agent is selected from direct thrombin inhibitors and pharamaceutically acceptable salts and prodrugs thereof, and fibrinogen receptor antagonists.

38. The method of claim 37 wherein said thrombin inhibitor is selected from boroarginine derivatives, boropeptides, hirudin derivatives and analogs thereof, and argatroban.

39. A pharmaceutically composition for treating a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa comprising a therapeutically effective amount of a Factor Xa-inhibiting pyrrolopyridine compound having the formula:



wherein Z is bonded to a pyrrolopyridine ring carbon atom, and one of X_5, X_{5a} and X_{5b} is an H, hydroxy, or amino substituent on the ring proximal to Z and attached at a carbon position that is adjacent to the carbon atom to which Z is attached and another of X_5, X_{5a} and X_{5b} is a substituent on the ring distal to the carbon atom to which Z is attached at a position alpha to the nitrogen on the distal ring and is selected from the group consisting of H, hydroxy, H_2N-, and (lower alkyl)HN-, wherein the lower alkyl is optionally substituted with an alkyl group substituent, (hydroxy)HN-, (alkoxy)HN- or (amino)HN-, the remaining one of X_5, X_{5a} and X_{5b} is a subsituent, as defined below, bonded to any one of the remaining carbon atoms of the pyrrolopyridine ring;

one of A_1, A_2 and A_3 is N and the other two are CH;

A_4 is NR_{11} and R_{11} is H, alkyl, aralkyl, heteroalkyl or $R_8(O)CCH_2$-;

Z is alkenyl, $-(CH_2)_r-C(O)NR"(CH_2)_s-$, $-(CH_2)_r-R"NC(O)(CH_2)_s-$ or $-(CH_2)_r-NR"(CH_2)_s-$, wherein R" is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl position with one or more ring system substituents and optionally substituted in the alkenyl proportion with one or more substiuents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally

substituted in the heteroaryl propor-tion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, wherein "r" is selected independently for each occurrence from 1 and 2 and "s" is selected independently for each occurrence from 0, 1, and 2;

R_1 is selected from (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) alkenyl, optionally substituted with one or more substituents selected from halogen and cycloalkyl; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (e) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) a member of the group consisting of $R'O(CH_2)_x$-, $R'O_2C(CH_2)_x$-, $R'C(O)(CH_2)_x$-, $Y^1Y^2NC(O)(CH_2)_x$, and $Y^1Y^2N(CH_2)_x$-, wherein Y^1 and Y^2 are independently: (a) hydro-gen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) heteroaryl, optionally substituted with one or more ring system; (e) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 member heterocyclyl, R'is (a) hydrogen; (b) alkyl optionally substituted with one or more alkyl group substituents; (c) aryl optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl portion with one or more ring systems substitutents and optionally substituted in the alkenyl

portion with one or more substituents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally syubstituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, and x=1,2,3,4 or 5;

R_2 is selected from: (a) hydrogen; (b) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (c) heteroaralkyl, optionally substitu-ted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (d) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selective from halogen and cycloalkyl; (e) heteroaralkenyl, optionally substituted in the heteroaryl por-tion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (f) a member of the group consisting of $R_3R_4NC(O)(CH_2)_x$-, $R_3S(O)p$-, and $R_3R_4NS(O)p$-, wherein: x is selected from 1, 2, 3, 4 and 5, and p is selected independently for each occurrence from 1 and 2;

R_3 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) cycloalkyl, optionally substitu-ted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroarayl; (d) heterocyclyl, optionally substituted with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl and fused heteroaryl; (e) aryl, optionally substituted with a ring system substituent; (f) heteroaryl, optionally substituted with a ring system substituent; (g) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group

substituents; (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more rings system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (i) aralkenyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (j) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl, or, optionally, R_1 and R_3 taken together with the –NS(O)p-moiety, the -S(O)p- moiety or the $-NR_4$- moiety through which R_1 and R_3 are linked form a 5 to 7 member heterocyclyl optionally substituted with one or more members selected from the group consisting of alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl substituents; and

R_4 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) cycloalkyl, optionally substitu-ted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroaryl; (d) aryl, optionally substituted with a ring system substituent; (e) heter-oaryl, optionally substituted with a ring system substituent; (f) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) hetero-aralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl group substituents, or, optionally R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a 4-7 member heterocyclyl, optionally substituted with one or more substituents selected from halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl;

X_1 and X_{1a} are independently selected from: (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (e) heteroaryl, optionally

substituted with one or more ring system substituents; (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, X_1 and X_{1a} taken together from oxo;

X_3 is selected from: H; (b) hydroxyl; (c) alkyl, optionally substituted with one or more ring system substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents, (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl groups substituents, or, optionally, X_3 and one of X_1 and X_{1a} taken together from a 4-7 member cycloalkyl;

X_4 is selected from (a) H; (b) alkyl, optionally substituted with one or more alkyl
groups substituents; and (c) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents;

one of X_5 and X_{5a} and X_{5b} which has not been otherwise selected is selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, R_5R_6NSO2-,
R_7CO-, halo, cyano, nitro and $R_8(O)CCH2$-;

R_5 and R_6 are independently selected from (a) H and (b) lower alkyl, optionally substituted with one or more alkyl group substituents; or one of R_5 and R_6 is H and the other is $R_8(O)CCH2$- or lower acyl;

R_7 is H, lower alkyl optionally substituted with one or more alkyl group substituents or $R_8(O)CCH2$-;

R_8 is selected from H, lower alkyl substituted with one or more alkyl group substituents, alkoxy and hydroxyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

and further comprising in a separate or combined formulation at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagelent agents, antiplatnet agents and fibrolinitic agents.

40. The pharmaceutical composition of claim 39 wherein said other agent is selected from standard heparin, low molecular weight heparin direct, thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

41. The pharmaceutical composition of claim 40 wherein said other agent is selected from direct thrombin inhibitors and pharamaceutically acceptable salts and prodrugs thereof, and fibrinogen receptor antagonists.

ATTACHMENT E

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	**Young Mi Choi-Sledeski, et al.**		
Application No.:	**09/918,039**	Examiner:	**T.N. Truong**
Filed:	**July 30, 2001**	Group Art Unit:	**1624**
For:	**SULFONIC ACID OR SULFONYLAMINO N-(HETEROARALKYL) AZAHETERYCYCLYLAMIDE COMPOUNDS**		

Attorney Docket No.: **P24,450-E US1**

Certificate of Mailing

I certify that this document is being deposited with the U.S. Postal Service as first class mail, postage prepaid, in an envelope addressed to the Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

June 30, 2006

Peter J. Butch III

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REPLY PURSUANT TO 37 C.F.R. § 1.111

In response to the outstanding Official Action mailed December 30, 2005, the following claim amendments and remarks are being submitted by Applicant for consideration by the Examiner.

Amendments to the Claims are reflected in the Listing of Claims, which begin on page 2 of this paper.

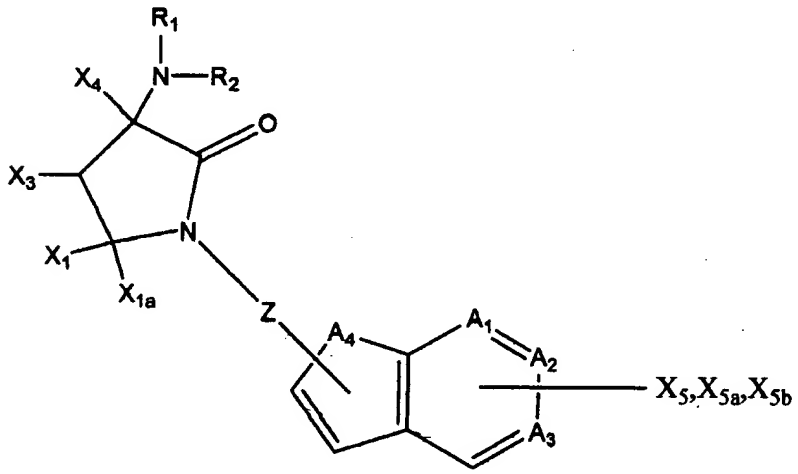
Applicant's **Remarks** begin on page 13 of this paper.

The Listing of Claims will replace all prior versions, and Listings, of claims in the application.

LISTING OF CLAIMS

Claims 1-34 (Cancelled).

Claims 35. (Currently Amended) A method for treating a patient suffering from a ~~physiological disorder~~ condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa comprising administering to the patient a therapeutically effective amount of a Factor Xa-inhibiting pyrrolopyridine compound having the formula:



wherein Z is bonded to ~~one of any carbon atom in a~~ pyrrolopyridine ring carbon atom ~~positions 2-7~~, and one of X_5, X_{5a} and X_{5b} is an H, hydroxy, or amino substituent on the ring proximal to Z and attached at a carbon position that is adjacent to the carbon atom to which Z is attached and another of X_5, X_{5a} and X_{5b} is a substituent on the ring distal to the carbon atom to which Z is attached at a position alpha to the nitrogen on the distal ring and is selected from the group consisting of H, hydroxy, H_2N- [[,]] and (lower alkyl)HN-, wherein the lower alkyl is optionally substituted with an alkyl group substituent, (hydroxy)HN-, (alkoxy)HN- or ~~and~~ (amino)HN-, the remaining one of X_5, X_{5a} and X_{5b} is a subsituent, as defined below, bonded to any ~~one~~ of the ~~remaining~~ carbon atoms ~~appearing at positions 2-7~~ of the pyrrolopyridine ring ~~moiety~~;

one of A_1, A_2 and A_3 is N and the other two are CH;

A_4 is NR_{11} and R_{11} is H, alkyl, aralkyl, heteroalkyl or $R_8(O)CCH_2$-;

Z is alkenyl, $-(CH_2)_r-C(O)NR"(CH_2)_s-$, $-(CH_2)_r-R"NC(O)(CH_2)_s-$ or $-(CH_2)_r-NR"(CH_2)_s-$, wherein ~~R' and~~ R" is selected from the group consisting of ~~are independently~~: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl position with one or more ring system substituents and optionally substituted in the alkenyl proportion with one or more substiuents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl proportion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, wherein "r" is selected independently for each occurrence from 1 and 2 and "s" is selected independently for each occurrence from 0, 1, and 2;

R_1 is selected from (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) alkenyl, optionally substituted with one or more substituents selected from halogen and cycloalkyl; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (e) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) a member of the group consisting of $R'O(CH_2)_x-$, $R'O_2C(CH_2)_x-$, $R'C(O)(CH_2)_x-$, $Y^1Y^2NC(O)(CH_2)_x$, and $Y^1Y^2N(CH_2)_x-$, wherein Y^1 and Y^2 are independently: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) heteroaryl, optionally substituted with one or more ring system; (e) aralkyl, optionally substituted in the aryl portion with one or more ring systems

substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 member heterocyclyl, R'is ~~as defined above~~ (a) hydrogen; (b) alkyl optionally substituted with one or more alkyl group substituents; (c) aryl optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl portion with one or more ring systems substitutents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally syubstituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, and x=1,2,3,4 or 5;

R_2 is selected from: (a) hydrogen; (b) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (c) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (d) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selective from halogen and cycloalkyl; (e) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (f) a member of the group consisting of $R_3R_4NC(O)(CH_2)_x$-, $R_3S(O)p$-, and $R_3R_4NS(O)p$-, wherein: x is selected from 1, 2, 3, 4 and 5, and p is selected independently for each occurrence from 1 and 2;

R_3 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) cycloalkyl, optionally substituted

with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroarayl; (d) heterocyclyl, optionally substituted with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl and fused heteroaryl; (e) aryl, optionally substituted with a ring system substituent; (f) heteroaryl, optionally substituted with a ring system substituent; (g) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more rings system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (i) aralkenyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (j) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl, or, optionally, R_1 and R_3 taken together with the –NS(O)p-moiety, ~~or~~ the -S(O)p- moiety or the $-NR_4$- moiety through which R_1 and R_3 are linked form a 5 to 7 member heterocyclyl optionally substituted with one or more members selected from the group consisting of alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl substituents; and

R_4 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroaryl; (d) aryl, optionally substituted with a ring system substituent; (e) heteroaryl, optionally substituted with a ring system substituent; (f) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl group substituents, or, optionally R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a 4-7 member heterocyclyl, optionally substituted with one or more substituents selected from halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl;

X_1 and X_{1a} are independently selected from: (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents; (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, X_1 and X_{1a} taken together from oxo;

X_3 is selected from: H; (b) hydroxyl; (c) alkyl, optionally substituted with one or more ring system substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents, (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl groups substituents, or, optionally, X_3 and one of X_1 and X_{1a} taken together from a 4-7 member cycloalkyl;

X_4 is selected from (a) H; (b) alkyl, optionally substituted with one or more alkyl groups substituents; and (c) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents;

one of X_5 and X_{5a} and X_{5b} which has not been otherwise selected is selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, R_5R_6NSO2-, R_7CO-, halo, cyano, nitro and $R_8(O)CCH2$-;

R_5 and R_6 are independently selected from (a) H and (b) lower alkyl, optionally substituted with one or more alkyl group substituents; or one of R_5 and R_6 is H and the other is $R_8(O)CCH2$- or lower acyl;

R_7 is H, lower alkyl optionally substituted with one or more alkyl group substituents or $R_8(O)CCH2$-;

R_8 is selected from H, lower alkyl substituted with one or more alkyl group substituents, alkoxy and hydroxyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

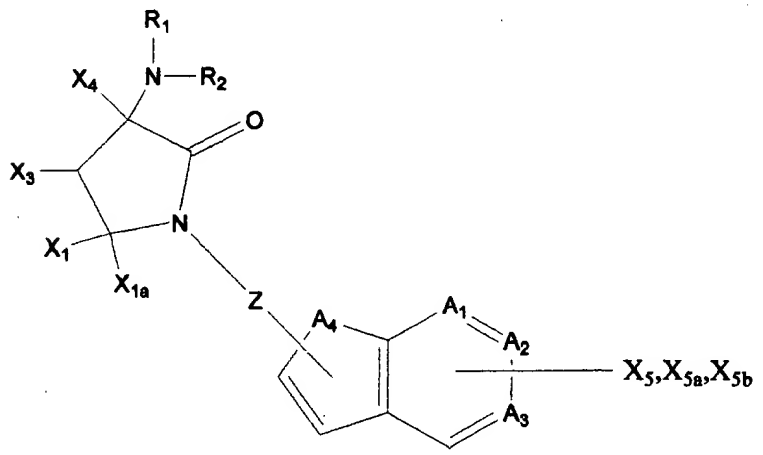
wherein said compound is administered in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinoloytic agents.

Claim 36. (Original) The method of claim 35 wherein said other agent is selected from standard heparin, low molecular weight heparin, direct thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

Claim 37. (Currently Amended) The method of claim 36 wherein said other agent is selected from direct thrombin inhibitors and pharamaceutically acceptable salts and prodrugs thereof, and fibrinogen receptor antagonists.

Claim 38. (Currently Amended) The method of claim 37 wherein said thrombin inhibitor is selected from boroarginine derivatives, boropeptides, hirudin derivatives and analogs thereof, and argatroban ~~and the pharmaceutically acceptable salts, prodrugs, derivatives and analogs thereof.~~

Claim 39. (Currently Amended) A pharmaceutically composition for treating a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa comprising a therapeutically effective amount of a Factor Xa-inhibiting pyrrolopyridine compound having the formula:



wherein Z is bonded to ~~one of any carbon atom in~~ a pyrrolopyridine ring carbon atom ~~positions 2-7~~, and one of X_5, X_{5a} and X_{5b} is an H, hydroxy, or amino substituent on the ring proximal to Z and attached at a carbon position that is adjacent to the carbon atom to which Z is attached and another of X_5, X_{5a} and X_{5b} is a substituent on the ring distal to the carbon atom to which Z is attached at a position alpha to the nitrogen on the distal ring and is selected from the group consisting of H, hydroxy, H_2N- [[,]] and (lower alkyl)HN-, wherein the lower alkyl is optionally substituted with an alkyl group substituent, (hydroxy)HN-, (alkoxy)HN- or ~~and~~ (amino)HN-, the remaining one of X_5, X_{5a} and X_{5b} is a subsituent, as defined below, bonded to any one of the remaining carbon atoms ~~appearing at positions 2-7~~ of the pyrrolopyridine ring ~~moiety~~;

one of A_1, A_2 and A_3 is N and the other two are CH;

A_4 is NR_{11} and R_{11} is H, alkyl, aralkyl, heteroalkyl or $R_8(O)CCH_2$-;

Z is alkenyl, -$(CH_2)_r$-C(O)NR"$(CH_2)_s$-, -$(CH_2)_r$-R"NC(O)$(CH_2)_s$- or –$(CH_2)_r$-NR"$(CH_2)_s$-, wherein ~~R' and~~ R" is selected from the group consisting of ~~are independently~~: (a) hydrogen; (b) alkyl, optionally substituted ~~with~~ one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl position with one or more ring system substituents and optionally substituted in the alkenyl proportion with one or more substiuents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl proportion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, wherein "r" is selected independently for each occurrence from 1 and 2 and "s" is selected independently for each occurrence from 0, 1, and 2;

R_1 is selected from (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) alkenyl, optionally substituted with one or more substituents selected from halogen and cycloalkyl; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (e) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) a member of the group consisting of $R'O(CH_2)_x$-, $R'O_2C(CH_2)_x$-, $R'C(O)(CH_2)_x$-, $Y^1Y^2NC(O)(CH_2)_x$, and $Y^1Y^2N(CH_2)_x$-, wherein Y^1 and Y^2 are independently: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) heteroaryl, optionally substituted with one or more ring system; (e) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; and (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 member heterocyclyl, R'is ~~as defined above~~ (a) hydrogen; (b) alkyl optionally substituted with one or more alkyl group substituents; (c) aryl optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl portion with one or more ring systems substitutents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally syubstituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, and x=1,2,3,4 or 5;

R_2 is selected from: (a) hydrogen; (b) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (c) heteroaralkyl, optionally substituted in the

heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (d) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selective from halogen and cycloalkyl; (e) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (f) a member of the group consisting of $R_3R_4NC(O)(CH_2)_x$-, $R_3S(O)p$-, and $R_3R_4NS(O)p$-, wherein: x is selected from 1, 2, 3, 4 and 5, and p is selected independently for each occurrence from 1 and 2;

R_3 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl groups substituents; (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroarayl; (d) heterocyclyl, optionally substituted with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl and fused heteroaryl; (e) aryl, optionally substituted with a ring system substituent; (f) heteroaryl, optionally substituted with a ring system substituent; (g) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more rings system substituents and optionally substituted in the alkyl portion with one or more alkyl groups substituents; (i) aralkenyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (j) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl, or, optionally, R_1 and R_3 taken together with the –NS(O)p-moiety, ~~or~~ the -S(O)p- moiety or the $-NR_4$- moiety through which R_1 and R_3 are linked form a 5 to 7 member heterocyclyl optionally substituted with one or more members selected from the group consisting of alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl substituents; and

R_4 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) cycloalkyl, optionally substituted

with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroaryl; (d) aryl, optionally substituted with a ring system substituent; (e) heteroaryl, optionally substituted with a ring system substituent; (f) aralkyl, optionally substituted in the aryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl group substituents, or, optionally R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a 4-7 member heterocyclyl, optionally substituted with one or more substituents selected from halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl;

X_1 and X_{1a} are independently selected from: (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring systems substituents; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents; (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, or, optionally, X_1 and X_{1a} taken together from oxo;

X_3 is selected from: H; (b) hydroxyl; (c) alkyl, optionally substituted with one or more ring system substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents, (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring systems substituents and optionally substituted alkyl portion with one or more alkyl groups substituents, or, optionally, X_3 and one of X_1 and X_{1a} taken together from a 4-7 member cycloalkyl;

X_4 is selected from (a) H; (b) alkyl, optionally substituted with one or more alkyl groups substituents; and (c) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents;

one of X_5 and X_{5a} and X_{5b} which has not been otherwise selected is selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, R_5R_6NSO2-, R_7CO-, halo, cyano, nitro and $R_8(O)CCH2$-;

R_5 and R_6 are independently selected from (a) H and (b) lower alkyl, optionally substituted with one or more alkyl group substituents; or one of R_5 and R_6 is H and the other is $R_8(O)CCH2$- or lower acyl;

R_7 is H, lower alkyl optionally substituted with one or more alkyl group substituents or $R_8(O)CCH2$-;

R_8 is selected from H, lower alkyl substituted with one or more alkyl group substituents, alkoxy and hydroxyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

wherein said compound is administered in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinoloytic agents;

and further comprising in a separate or combined formulation at least one other agents selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagelent agents, antiplatnet agents and fibrolinitic agents.

Claim 40. (Original) The pharmaceutical composition of claim 39 wherein said other agent is selected from standard heparin, low molecular weight heparin direct, thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

Claim 41. (Currently Amended) The pharmaceutical composition of claim 40 wherein said other agent is selected from direct thrombin inhibitors and pharamaceutically acceptable salts and prodrugs thereof, and fibrinogen receptor antagonists.

Claim 42. (Cancelled)

REMARKS

This amendment is submitted in response to the Official Action mailed Dec 30, 2005. In view of the above claim amendments and the following remarks, reconsideration by the Examiner and allowance of the application is respectfully requested.

Claims 35, 37-39 and 41 have been amended to more particularly point out and distinctly claimed the subject matter that applicants regards as the invention. In particular, claim 35 has been amended to clarify that the treatment method is for treating a patient suffering from a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa with a Factor Xa-inhibiting pyrrolopyridine compound. Claim 39 has been similarly amended to clarify that the composition is for treating a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa and contains a therapeutically effective amount of a Factor Xa-inhibiting pyrrolopyridine. This is disclosed in the specification at page 1, lines 26-27 and does not introduce new matter to either claim.

Claims 35 and 39 have both also been amended to clarify that Z is bonded to a pyrrolopyrdine ring carbon atom. This is shown generally through out the specification and also does not introduce new matter. Claims 35 and 39 have also been amended to claim pharmaceutically acceptable salts, N-oxides, hydrates and solvates of the pyrrolopyridine compound. This was a limitation of original claim 1 and therefore also does not introduce new matter. Claims 35 and 39 have also been amended to correct various typographical errors without introducing new matter. Finally, claim 39 has further been amended to clarify that the additional agents of the pharmaceutical composition are formulated in a separate or combined formulation with the pyrrolopyridine compound. This is disclosed in the specification at page 173 lines 28-30 and also does not introduce new matter.

In addition, claims 37 and 41 have been amended to clarify that the direct thrombin inhibitors include pharmaceutically acceptable salts and prodrugs thereof. This is disclosed in the specification in the last line of page 172 and does not introduce new matter. Finally, claim 38 has been amended to clarify that hirudin includes hirudin derivatives and analogs thereof. This is disclosed in the specification at page 173, lines 3-4, and also does not introduce new matter.

In view of the above claim amendments, the within application is believed to be in condition for allowance. Reconsideration of the rejections made by the Examiner is therefore respectfully requested.

Turning to the Official Action, claims 35-41 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention. In particular, the Examiner considered the language "a physiological disorder capable of being modulated by inhibiting an activity of Factor Xa" in claim 35 to be indefinite because it reads on disorders with too little clotting and disorders with too much clotting, and because the specification also associated Factor Xa "with more diseases than just blood coagulation." Claims 35 and 39 were also considered indefinite by the Examiner for reciting the positions of Z as "positions 2-7" on the pyrrolopyridine ring when the specification did not number the pyrrolopyridine ring consistent with the way recognized by the art. The Examiner also considered claim 39 indefinite because it was not clear if the additional agents were formulated in the same composition with the pyrrolopyridine compound, or if the additional agents were in a separate formulation. Finally, the Examiner rejected claim 38 for lacking antecedent basis because it depends from claim 35 but recites "prodrugs, derivatives and analogs thereof," which are not recited in claim 35. These rejections are respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

Claim 35 has been amended to clarify that the claimed method in treating a patient suffering from a condition of the arterial or venous vasculature capable of being modulated by inhibiting an activity of Factor Xa. The conditions intended for treatment are readily identified by one having ordinary skill in the art. The diseases intended for treatment by the method of claim 35 are now clear. By amending claim 35 in this manner, this portion of the rejection of claims 35-38 as indefinite under 35 U.S.C. § 112, second paragraph has been traversed.

Claim 35 has also been amended, as well as claim 39, to clarify that Z is bonded to a pyrrolopyridine ring carbon atom, instead of referring to a numbered ring position. The ring atoms to which Z may be bonded are now clear to one of ordinary skill in the art. By amend-

ing claims 35 and 39 in this manner, this portion of the rejection of claims 35-41 as indefinite under 35 U.S.C. § 112, second paragraph has also been traversed.

Claim 39 has also been amended to clarify that the additional agents of the pharmaceutical composition are in a separate or combined formulation with the pyrrolopyridine compound. The metes and bounds of this feature of the claimed pharmaceutical composition are now cleared to one of ordinary skill of the art. By amending claim 39 in this manner this portion of the rejection of claims 39-41 as indefinite under 35 U.S.C. §112, second paragraph has been traversed.

Regarding the rejection of claim 38, this claim depends directly from claim 37 and only indirectly from claim 35. A review of the specification reveals that pharmaceutically acceptable salts and prodrugs refer to the direct thrombin inhibitors of claim 37, and the derivates and analogs refers to hirudin. Accordingly, claims 37 and 38 have been amended so they are now consistent with the specification. Claim 41, which corresponds to claim 37, has been similarly amended.

While claims 35 and 36, from which claims 37 and 38 directly or indirectly depend, do not recite pharmaceutically acceptable salt, prodrugs, derivates and analogs, the direct thrombin inhibiting agents and inhibitors referred to in claims 35 and claims 36 are generic to pharmaceutically acceptable salts and prodrugs of direct thrombin inhibitors. Likewise, hirudin and hirudin derivatives and analogs thereof are also species of the direct thrombin inhibiting agents and inhibitors of claims 35-37.

Amended claims 37 and 38 therefore do not lack antecedent basis for the recited claimed terms. This portion of the indefiniteness rejection under 35 U.S.C. § 112, second paragraph has thus also been traversed.

By amending claims 35, 37-39 and 41 to clarify the conditions being treated, the positioning of the Z group on the pyrrolopyridine ring, the additional agents for which pharmaceutically acceptable salts, prodrugs, derivatives and analogs thereof are being claimed, and the formulation of the pyrrolopyridine compound and additional agent in either separate or combined formulations, this rejection of claims 35-41 as indefinite under 35

U.S.C. § 112, second paragraph has thus been overcome. Reconsideration by the Examiner and withdrawal of this rejection is therefore respectfully requested.

Next, claims 35-41 were rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. In particular, the Examiner considered the recited combinations of compounds for treating "a physiological disorder capable of being modulated by inhibiting an activity of Factor Xa," which include more than anticoagulant therapy, to be "unduly broad." The Examiner also considered claim 39 to be unduly broad because it recited the same combination of pyrrolopyridine compounds and additional agents as that recited in claim 35. The Examiner considered the claimed combination "unduly broad" without regard to the indication that the combination was intended to treat. This rejection is respectfully traversed in view of the above claim amendments for the reasons set forth hereinafter.

The breadth of the independent claims are now limited to a scope for which adequate direction and guidance is presented in the specification in view of the state of the art related to Factor Xa inhibitors. Regardless of the activity other pyrrollopyridine compounds have, the pyrrolidinone-pyrrolopyridine molecular core identified by the Examiner is reported by Applicant to have Factor Xa inhibiting activity. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. § 112, first paragraph. (See MPEP §2164.01(c)).

That is, the enablement of how to practice the claimed treatment method with the claimed pharmaceutical compositions is not evaluated relative to compounds with similar structures, it is evaluated relative to compounds with similar activity. For the treatment of Factor Xa modulated conditions of the arterial or venous vasculature, undue experimentation is not required for one of ordinary skill in the art guided by the present specification to apply the presently claimed pharmaceutical composition to the presently claimed treatment method by comparison of the inhibitory activities of the inventive compositions to other known Factor Xa inhibitor compositions. Amended claim 35 is thus directed to treatment methods adequately enabled by the teachings of the specification viewed in the context of the Factor

Xa inhibitor state of the art. In view of the Factor Xa state of the art, amended pharmaceutical composition claim 39 is adequately enabled as well.

Claims 35-41 therefore satisfy the enablement requirements of 35 U.S.C. §112, first paragraph as it relates to Factor Xa inhibiting compositions and treatment methods. By amending claim 35 so it is now directed to a method for treating a patient suffering from a Factor Xa modulated condition of the arterial or venous vasculature, and similarly amending claim 39, this rejection of claim 35-41 for lack of enablement under 35 U.S.C. §112, first paragraph has thus been overcome. Reconsideration by the Examiner and withdrawl of this rejection is therefore respectfully requested.

In view of the above claim amendments and the foregoing remarks this application is now in condition for allowance. Reconsideration is respectfully requested. The Examiner is requested to call the undersigned at the telephone number indicated below if there any issues remaining in this application to be resolved. Finally, if there are any additional charges in connection with this response, the Examiner is authorized to charge Applicants' Deposit Account No. 19-5425 therefor.

Respectfully submitted,

June 30, 2006

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